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Malignant Pericardial Effusion in Breast Cancer: Terminal Event or Treatable Complication?

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Background: Few data are available on malignant pericardial effusion (MPCE) in breast cancer. We identify the patient prone to develop MPCE, describe the result of surgical management, and try to identify a subgroup of patients who do not benefit from surgical management.
Method: We performed an audit of our policy of active search for MPCE in breast cancer patients and its treatment by subxiphoid pericardial fenestration.
Result: Nineteen patients with MPCE had a mean of 3.2 other sites of recurrence; 17 had pleural recurrence. Six patients had exertional dyspnea and 13 had dyspnea at rest; three needed emergency pericardiocentesis. An average of 740 ml of fluid was recovered; cytology was diagnostic in 11 cases and histopathology in 10 cases. At discharge, six patients had no dyspnea and six had exertional dyspnea. Of 10 patients who did not receive systemic treatment, eight died within 30 days. Nine patients who received systemic treatment had an average survival of 8.3 months.
Conclusions: Patients with pleural recurrence presenting with dyspnea should be evaluated for the presence of a MPCE. Subxiphoid pericardial fenestration is the treatment of choice. Patients who will not receive systemic treatment should be managed conservatively.
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KEY WORDS: breast cancer; metastases; pericardial window; tamponade

INTRODUCTION

Malignant pericardial effusion (MPCE) is a known complication of advanced malignancy [1–11]. In an autopsy series of patients with breast cancer, pericardial disease was found in 19% of cases and thought to be the immediate cause of death in 4% [12]. In that series, only three of 37 cases of cardiac/pericardiac involvement with tumour were diagnosed ante mortem. In another series of PCE in breast cancer, about half of the cases were diagnosed at autopsy only [13]. Added to the difficulty of diagnosing pericardial involvement during life is the paucity of clinical data on breast cancer patients with pericardial involvement. Only a few small series have reported on pericardial effusions in breast cancer [13–17]. These describe the efficacy of treatments in eliminating the effusion and preventing its recurrence. MPCE is a complication of advanced disease with no chance of cure, and symptomatic relief should be the most important determinant of successful treatment. In this study, we concentrate on symptomatic, pathologically proven MPCE in breast cancer. We describe the patient prone to develop this complication and report the results of pericardial fenestration with respect to symptom relief, morbidity, and mortality. We try to identify a group of patients who will not benefit from active surgical management.

MATERIALS AND METHODS

Since 1987, all breast cancer patients who presented with dyspnea were subjected to echocardiographic evalu-

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TABLE I: Stage at Diagnosis of Breast Cancer and Time to Development of Malignant Pericardial Effusion

Stage	Number of patients	Average time to development of MPCE (months)
I	1	46
II	6	38
III	8	23
IV	3	39

ation of the pericardium after exclusion or correction of other obvious causes of dyspnea, such as anaemia, pleural effusion, lymphangiitis, and pneumonitis. Effusions with <1.0 cm posterior separation during diastole were considered small; effusions with >1 cm posterior separation during diastole or anterior separation of epicardium and pericardium were considered large.

All patients with pericardial effusions had subxiphoid pericardial fenestration according to the technique described by Fontanelle et al. [18]. Pericardial biopsies were sent for histopathological evaluation. Pericardial fluid was collected as completely as possible, the volume measured, and the entire specimen sent for cytopathological evaluation.

For this report, only data from patients who had pathological proof of malignancy were analysed. Dyspnea was quantified as follows: grade I: no dyspnea, grade II: exertional dyspnea, grade III: dyspnea with daily routine and grade IV: dyspnea at rest. Dyspnea was recorded preoperatively, at discharge from the hospital and with every follow-up visit. Perioperative morbidity and mortality were recorded. Age and sex of patients as well as data concerning staging, pre- and postoperative treatments, and survival were retrieved from our prospective breast cancer data base. Survival was calculated according to the method of Kaplan and Meier [19].

RESULTS

A total of 2,700 new patients since 1987 have been treated for pathologically confirmed breast cancer at the Breast Clinic of the University of Stellenbosch. Of these patients, 19 presented to our clinic with symptomatic MPCE for a crude incidence rate of 0.7%. Their mean age at diagnosis of breast cancer was 44 years (range: 27–67). Half of them were premenopausal. The primary tumour was leftsided in 11 cases. The stage at diagnosis and the time to development of MPCE are given in Table I.

Systemic treatment options had been exhausted in 10 patients at the time of presentation with MPCE (Table II) and patients had a mean of 3.2 other sites of recurrence. Details of the sites of recurrence are given in Table III. Six patients presented with grade III dyspnea and 13 patients with grade IV dyspnea. Seventeen patients had large pericardial effusions. Three patients needed emergency pericardiocentesis for hemodynamic instability. At pericardial fenestration, an average of 740 ml of pericardial fluid was recovered. Cytology was positive for malignant cells in 11 cases. Histopathology of the pericardial biopsy was reported as metastatic carcinoma in 10 cases.

TABLE II: Patients in Whom Systemic Therapeutic Options Had Been Exhausted: Treatment since Diagnosis of Breast Cancer Until Development of Malignant Pericardial Effusion*

Chemotherapy	
Cyclophosphamide, methotrexate and 5-fluorouracil (CMF);	
Cyclophosphamide, Adriamycin and 5-fluorouracil (CAF);	CMF + CAF − 8 patients
Methotrexate, mitomycin C and mitoxantrone (MMM)	CMF + CAF + MMM − 1 patient
Hormonal therapy	
Bilateral salpingo-oöphorectomy (BSO);	BSO − 2 patients
Tamoxifen (TAM);	TAM + AMI − 3 patients
Aminoglutethimide (AMI)	BSO + TAM + AMI − 1 patient
	TAM − 1 patient

*One patient was initially treated at another institution and had both chemotherapy and hormonal therapy. We have no specific information regarding this treatment.

None of the following factors predicted an unfavourable outcome: patient age at diagnosis of breast cancer, menopausal status, stage at diagnosis of breast cancer, prior radiotherapy to breast or chest wall, number of sites of metastatic disease, degree of dyspnea at diagnosis of MPCE, necessity for emergency pericardiocentesis or the volume of the pericardial effusion.

Of 10 patients in whom systemic treatment options had been exhausted, four patients died within 24 hours of pericardial fenestration. The cause of death was progressive cardiac failure resistant to maximal inotropic support in three patients and sudden cardiac death in one patient. Four other patients died within 30 days of the procedure for a combined 30-day mortality rate of 80%. Two patients survived for 37 days and for 6 months before succumbing to progression of their disease.

TABLE III: Sites of Metastatic Involvement at Time of Presentation With Malignant Pericardial Effusion

Site	Patients (n)
Pleural effusion	Unilateral:10 Bilateral: 7
Bone	12
Lung	9
Lymph nodes	9
Local recurrence	7
Liver	3
Soft tissue	3
Brain	1

None of the patients in whom systemic treatment options still existed died within 30 days of the operation. Average survival for these patients was 8.3 months with a minimum of 2.3 months, and one patient was still alive at 19 months postoperatively. Four patients received chemotherapy and five received hormonal treatment.

At discharge from the hospital, six patients had grade I dyspnea and six grade II dyspnea. None of the patients had recurrence of their pericardial effusions either on short- or long-term follow-up. One patient was lost to follow-up after 3 months.

DISCUSSION

MPCE is a complication of advanced breast cancer [13–17]. Similar to other series, none of our patients had MPCE as an initial manifestation of metastatic disease. Pleural or lung metastases prior to or concomitant with MPCE have been described for a high percentage of patients presenting with MPCEs in general [2,7]. In breast cancer, an incidence of 63–100% [13–17] of lung and pleural metastases were found at the time of diagnosis of pericardial effusions. In our series, 17 of 19 patients (89%) had pleural effusions. Pleural effusion precedes or accompanies MPCE in almost every case, with a high incidence of bilaterality. The two patients without pleural effusions had received radiotherapy to the chest wall or breast. We have shown previously that this prevents the development of ipsilateral pleural effusions [20]. All patients with dyspnea not responding symptomatically to drainage of pleural effusions should be evaluated promptly for the presence of a pericardial effusion.

At this stage of the disease process, symptomatic relief should be the most important determinant of success of therapeutic intervention. Thirteen patients evaluated postoperatively had their independence restored from permanent assistance. Surgical construction of a pericardial window enabled them to manage their daily routine without becoming dyspneic. All six patients in the series of Bitran et al. [16] had complete resolution of their symptoms after pleuropericardial fenestration.

In the available series [13–17] of pericardial effusion in breast cancer, a variety of local treatments were applied. In patients with pathologically proven MPCE, Buck et al. [13] reported no deaths within 30 days in nine patients treated surgically (pericardiectomy or fenestration). All three patients initially treated by pericardiocentesis relapsed; two then had definitive surgical treatment and one patient died of the recurrent pericardial effusion. The mean survival after treatment of MPCE was 19 months with all patients receiving additional systemic therapy. Woll et al. [14] treated 22 patients with pericardial tamponade by pericardiocentesis. Four patients required additional procedures to control the effusions. Median survival was 13 months. The etiology of the effusions or the morbidity of their treatment approach was not specified. We suspect that many effusions in their series were of benign etiology, explaining the low recurrence rate. Edoute et al. [15] treated 13 patients with MPCE with initial pericardiocentesis. Three of these patients developed a recurrence of their effusion and were treated by pericardiectomy. They had a mean survival of 22.3 months. Patients not subjected to surgery had a mean survival of 4.7 months. Morbidity is not specified in their study. Bitran et al. [16] treated six patients by pleuropericardial fenestration. None of their patients had recurrence of pericardial effusions. Two patients who did not have systemic therapy postoperatively survived 1 and 5 months. Four patients who did receive systemic therapy survived an average of 32 months. All three patients of Reynolds and Byrne [17] received systemic therapy after pericardiocentesis; the survival is not given in their study.

About 44% of MPCEs treated by pericardiocentesis alone will recur [11]. Subxiphoid pericardial fenestration allows for collection of specimens for both cytopathological and histopathological examination, increasing the diagnostic accuracy. In our study there was a low sensitivity when either examination was used individually with only two patients having both cytology and histopathology positive for metastatic disease. Creation of a pericardial window can be performed with little morbidity and is very effective in the permanent control of MPCE [4,10,11,22]. The 30-day mortality rate in our series is high. Our active search for the presence of MPCE may have identified patients in whom the pericardial effusion was rather an incidental finding in the terminal stages of the disease process and other causes of death supervened. This is in accordance with an autopsy series of patients with breast cancer in which pericardial involvement was felt to be the cause of death in only one-fifth of the cases in which it was diagnosed [12].

Except for the availability of systemic treatment options, clinical parameters do not permit selection of patients for active management. We propose that patients in whom systemic treatment options are still available should undergo subxiphoid pericardial fenestration. Patients in whom systemic treatment options have been exhausted have a very poor prognosis and should be managed conservatively, e.g., by pericardiocentesis under echocardiographic guidance [9,21].

CONCLUSION

Patients with known breast cancer presenting with dyspnea should be evaluated for MPCE when other causes of dyspnea have been excluded. Operative management gives good long-term relief with low morbidity. Patients in whom systemic treatment options have been exhausted should be managed conservatively.

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